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EDITORIAL

3T3.

With the closing of this term and the ceremonies of graduation the class of '33 Medicine, University of Toronto, passes into the great body of graduates of the University. At the first of every term one's mind turns toward the incoming freshmen, whereas in the spring the thoughts of all are associated with the graduating Seniors. The time of graduation represents at once the severance of undergraduate activities and associations and the beginning of one's more or less "independent" existence. The graduating year leaves the undergraduate friendships, the systematized process of education and the more or less strict discipline of a medical school to enter upon the sphere of broader professional interests, an individualistic method of continuing one's education and a discipline, the degree of strictness of which depends upon one's desire. It has many times been the advice of older members of the profession upon the occason of graduation that the men embarking upon their career ever remain ardent students of medicine. We can but reiterate this. There is no one in the graduating year but feels his inability before the mountain of medical knowledge which confronts him. We believe that it is the deep-rooted hope of every member of the graduating class that he will ever remain a student—not a mere book-learner, but a keen student of medicine in every sense of the term.

The graduate of '33 has not the most propitious opportunities at the time

of graduation. It is realized that the physician beginning his life-work at the present time will have a much greater handicap than had those a few years past. However, as a prominent member of the profession has said, a man equipped with a medical education is more fortunate even in times of adversity than almost any other person. Even though one may not have the privilege of accomplishing all that he desires from a financial standpoint, he has at least the satisfaction of having something worth doing and worthy of his best efforts.

May 3T3 Medicine continue to uphold the traditions so richly held by our distinguished body of graduates!

THE PRESENT KNOWLEDGE OF INFANTILE PARALYSIS.

The state of our knowledge of Infantile Paralysis was presented in a paper by Dr. William H. Park of the New York City Health Department to the American Association for the Advancement of Science:

"In the majority of those infected with the causative virus of the disease, the central nervous system is not invaded, or, if it is, the injuries do not progress sufficiently to lead to paralysis.

The value of convalescent serum for treatment is rather dubious, it appears from studies which Dr. Park reviewed. In the epidemic of 1931, investigators in Boston and New York found that the cases which did not receive serum treatment got along slightly better than those receiving it.

The increased amount of infantile paralysis seems to be due to the fact that more and more people are passing from one place to another; so the opportunity is increased of a fully virulent virus being spread to localities where the disease has not occurred before and where there is more or less virgin soil for the virus to infect.

There are more cases of the disease and more frequent epidemics in colder countries, with the important exception of China.

In the same latitude, there is apparently very little difference in the disease rate between cities and countryside.

The value of serum as a protective agent for at least four weeks was shown in an experiment made by a former member of Dr. Park's staff, the late Dr. William Brebner. He gave serum to twelve hundred children in a town in which there was an outbreak of the disease. In the same town, eighteen hundred children were not immunized to the disease. Within the next two weeks, thirty-one cases occurred in those not immunized."

DR. RONALD STEELE SADDINGTON.

RONALD STEELE SADDINGTON, M.D., B.Sc. (Med.)

AN APPRECIATION

By T. H. BELT, M.B., B.Sc. (Med.)

TO the many friends and colleagues of Doctor Ronald Steele Saddington, the tragic news of his untimely death came as a great shock. Doctor Saddington was engaged in researches upon the problem of filterable viruses, working under Doctor Simon Flexner at the Rockefeller Institute in New York, when, between Christmas and New Year's last, he contracted a mild infection from some material with which he was working. For several days his condition caused no alarm. Then a thrombo-phlebitis developed in the veins of one leg, and from that time on his illness took a stormy course, with

(*Photograph by Milne Brothers.*)

pulmonary embolisms occurring at intervals. The fatal embolism occurred on February 4th, just at a time when it was thought that he was finally out of danger.

Born in Almonte, Ont., in 1902, a son of the Venerable Archdeacon and Mrs. C. Saddington (now of Port Credit), Doctor Saddington graduated in Medicine from the University of Toronto in 1927. He was a member of Lambda Chi Alpha Fraternity, and had a host of warm friends among the staff and students. After a year of post-graduate work in clinical medicine in Cleveland, he returned to his Alma Mater to take a Fellowship in Pathology. He remained in this department for a period of three years, the last year of which he was a lecturer. During this time he found ever-increasing favour amongst those with whom he came in contact, and won distinction for his hard work. Many recent graduates will have happy recollections of him as a demonstrator and teacher. So happily did he impress himself upon his students, that he became the recipient of more than one handsome memento from them. Many are the individuals who will remember with pleasurable feelings his cheery presence in the lab, the class rooms, or at the autopsy table; he was painstaking, conscientious and skillful, but, above all, a likeable chap.

In the summer of 1931 he left Toronto to take up his work at the Rockefeller Institute. Of his work and his associates in New York he always spoke with great enthusiasm. Pure research was ever a joy to him, for he had a flare to seek out hidden truths, and he found in his New York post opportunities which engrossed him. His was a future more than usually bright, full of untold worth; a future, certainly, which could have yielded nothing but good to his fellow men.

It was more than an ordinary pleasure to have known Ronald Saddington. He was a rare, good fellow, possessed of many unusual and endearing qualities, for which his memory will long be cherished. He had a ready sense of humour and a handy philosophy which, at all times, seemed to elevate him above the petty meannesses of life. One could not wish for a finer companion in work or at play. A man of exemplary mien, happily adjustable to his surroundings, of an even, buoyant temperament, enthusiastic, conscientious almost to extremes., he was possessed of that ill-defined yet priceless attribute — the love of life.

His passing is a great loss, more keenly felt, perhaps, because his perennial vigour and cheeriness seemed of an enduring quality, invulnerable to such tragic accidents as that which caused his death. May the members of his family, to whom he was devoted, find some comfort in the thought that there are many who mourn with them the loss of one whose sterling qualities are not often equaled.

THE PRICE OF DELAY IN THE DIAGNOSIS OF UROLOGIC CONDITIONS

GORDON S. FOULDS, M.D., M.S., F.R.C.S. (C.).

The present trend of surgical practice is distinctly toward greater conservatism, and in no branch of surgery is this more marked than in urology. This aim is frustrated, altogether too frequently, by delay in diagnosis. Patients are commonly seen with extensive bladder tumors who have had haematuria for several months, or even years, and kidney stone cases seek treatment, in many instances, only after extensive renal damage has taken place, and in many cases nephrectomy is indicated where at an earlier date the stone might have been removed without sacrificing the kidney. Instances of this sort force one to ask why such delay should take place. The answer is not simple, but perhaps by citing and discussing some illustrative cases I can indicate the difficulties and failures in diagnosis, and so point the way to earlier and more complete investigation.

In renal tuberculosis the delay in diagnosis is usually due to failure to appreciate the significance of persistent frequency of urination and dysuria in young adults. This is illustrated by the following case history: Miss J. D., age 17 years, was referred to me complaining of frequency of urination of eighteen months' duration. The frequency had not responded to any form of medical treatment, but had become distinctly worse during the six weeks prior to the time she consulted me, at which time she was required to urinate every half hour during the day and several times each night. For four months blood had been seen in the urine at intervals. There was no cough.

Physical examination was essentially negative. There was no clinical evidence of pulmonary tuberculosis, though radiographic examination of the chest showed evidence of bilateral minimal tuberculous lesions. Urinalysis revealed an acid urine of 1018 specific gravity, with a trace of albumin present. Microscopic examination showed many pus cells and a few red blood cells. Tubercle bacilli were found on direct smear.

Cystoscopic examination showed an ulcerative cystitis typical of tuberculosis about the left ureteral orifice, and an almost functionless pyonephrosis in the left side. Tubercle bacilli were demonstrated in direct smear from the left ureteral urine. The urine from the right kidney contained an occasional pus cell, but no organisms were demonstrated on smear. The right pyelogram was normal. However, a guinea pig inoculated with urine from the right side developed tuberculous lesions.

After careful consideration, the left kidney was removed. The kidney showed an old ulcero-cavernous lesion involving principally the upper pole, and in addition recent tubercles scattered through the cortex. The patient, after an uneventful recovery from the operation, went to sanatarium. Her subsequent course, however, was unsatisfactory. She developed a generalized miliary tuberculosis and died about a year afterwards.

It seems probable that had an early diagnosis been made, an early nephrectomy would have removed the major focus of tuberculous infection before the exacerbation occurred, which probably was associated with the occurrence of the multiple tubercles in the left kidney. These were evidently duplicated in the right kidney and elsewhere in a miliary tuberculosis.

Benign hypertrophy of the prostate is encountered in a very large proportion of men past middle age. Consequently the commoner symptoms of the

condition are frequently looked upon as a normal state of affairs in older men, and they are often disregarded until well advanced systemic changes have taken place as a result of urinary retention. Therefore, the man past middle age with enlargement of the prostate, who develops distressing symptoms such as marked frequency and difficult urination, or even acute retention, early in the course of the process, is fortunate indeed. He is forced to seek relief from the urinary retention before serious renal damage has taken place. On the other hand, one sees cases such as that of an old gentleman who had noted some difficulty in urinating over a period of many years, but only sought the advice of his physician when nausea and anorexia became annoying. On enquiry into his history, his physician correlated these complaints with his urinary difficulty, and on examination found a chronically overdistended bladder, extending almost up to the umbilicus, and a greatly enlarged prostate. Renal function was greatly impaired. After gradual decompression of his bladder, and a two stage prostatectomy, with a long period of delay between the suprapubic cystostomy and the removal of the prostate, he is now convalescent and free from both local and general symptoms.

Patients seen early with a small amount of residual urine and only slight kidney damage, may be dealt with according to the type of obstruction, by transurethral prostatic resection, or suprapubic prostatectomy, with much greater safety and a much shorter period of incapacity, than those in whom marked systemic changes have taken place.

The most common cause of painless intermittent haematuria is a neoplasm in the bladder. Haematuria is generally looked upon by the patient as an alarming symptom. Yet in three separate series of cases which I have reviewed, I have found in each group that the average time to elapse between the first appearance of blood in the urine and investigation was about one year. It is difficult to realize what changes may take place in a carcinoma of the bladder in one year. A tumor which was small and had not infiltrated the bladder wall will have increased in size and extended by infiltration, so that it will have become converted from a tumor which could have been destroyed by electro - coagulation through the cystoscope, or successfully dealt with by resection, to one which is evidently inoperable or in which only palliative procedures are possible.

The delay is accounted for principally by the fact that the haematuria in these patients is intermittent. It clears up spontaneously, independently of any medication which may receive the credit for a cure, while the underlying condition progresses. On account of this peculiarity in haematuria due to bladder tumors, it is rare to see an early case of bladder neoplasm.

Why is it that many renal calculi go unrecognized for long periods of time? I think this is due to the fact that we are looking for a typical history of renal colic associated with haematuria, before suspecting the presence of a stone, and before considering a roentgen ray examination of the urinary tract. Truly, a very large proportion of patients suffering from stone do give a very suggestive history, but this is no reason for overlooking many of the less typical cases.

A case of this sort was Mr. H. M., aged 31, who was referred to me on account of pyuria. Attention was attracted to the presence of pyuria in 1918, during treatment at a prophylactic station in France. No venereal disease was contracted, but from this time on pus was present in the urine. One year later, and again in two years, a mild left epididymitis occurred. These attacks increased suspicion of latent gonorrhoea. A few years later an incomplete cystoscopic examination was made, with negative findings. No X-ray films were made at this time. During 1928, and later in the summer of

1929, attacks of unexplained malaise with chills and fever were experienced. On admission the physical examination was negative, except for marked pallor. Severe secondary anaemia was shown by a red blood cell count of 2,155,500 with haemoglobin of 32 per cent. A well marked reduction in renal function was demonstrated by high nitrogen retention in the blood, the blood urea nitrogen being 62.4 milligrams and non-protein nitrogen 93.5 milligrams for each 100 c.c. of blood, and a phenolsulphonephthalein secretion of 10.4 per cent. in two hours. The water test gave a fixed specific gravity with only four points variation after ingestion of 1,500 c.c. of water. A urine examination showed a specific gravity of 1012, the presence of a moderate amount of albumin and no sugar. Microscopic examination of the urine showed 200 to 300 pus cells per high power field.

Roentgenogram of the urinary tract showed extensive bilateral calculi, together with stones in the prostate, these latter probably accounting for the occurrence of the epididymitis.

It was apparent that little could be done for this young man. Operation was advised, but after considering the risks involved, both he and his parents refused to proceed with the removal of the calculi. He died about a year later. Had an earlier diagnosis been made, operation might have been carried out with relative safety. Other cases could be cited in which the chief complaint was haematuria following exertion, or atypical pain, in which kidney stone was the underlying condition.

In each of the conditions referred to, definite symptoms and physical signs were present for a considerable period of time, which if they had received proper consideration would have led to adequate investigation and correct diagnosis of the underlying conditions months or years earlier. In every case the price of such delay was apparantly high. Similar examples might be cited in carcinoma of the prostate, neoplasms of the kidney, urethral stricture and other urologic conditions. The following conclusions are justified:

(1) Every patient with haematuria should be investigated without delay.

(2) In every patient showing persistent pyuria, the source should be sought and the cause determined.

(3) Persistent frequency of urination with pyuria in a young adult should always arouse the suspicion of urinary tuberculosis.

(4) Frequency and difficulty of urination in men past middle age, though not unusual, is always associated with abnormality, which usually requires relief, and which, if neglected, may lead to extensive and serious systemic changes.

(5) It is abundantly demonstrated that the price of delay is not only great but is unjustified.

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OBESITY AND CHRONIC GALL BLADDER DISEASE

K. B. SCHLOTZAUER, M.D. (Toronto, '32), Ottawa Civic Hospital.

A rather typical case report of Chronic Cholecystitis with Cholelithiasis in an obese female patient is presented. At attempt to correlate symptoms, physical findings, with laboratory and X-ray methods has been made, with the purpose of treating the patient herself and not dealing solely with the diseased organ which has brought her to hospital.

A woman aged 42, of French parentage, was admitted to hospital on November 1st, 1932. Her complaints were belching of gas, indigestion, and severe colicky pains occurring in attacks of a varying duration. The above symptoms were intermittently present for the past twelve years. During this period she had suffered upper abdominal discomfort, belching of gas and a sensation of bloating following meals, without regular periodicity. Occasionally, she experienced feelings of nausea, of faintness and of regurgitation into the mouth. Slight chilly sensations occurred at times. At intervals varying in time (a few weeks to a few months) and intensity, she suffered a more severe gastric disturbance associated with considerable vomiting and having a distressingly similar type of pain. The attack usually set in rather abruptly, with agonizing pain in the upper right abdomen, and described as going "straight through" to the right shoulder. These attacks persisted sometimes for twenty or thirty minutes, and other times for several hours, and were followed by a feeling of soreness in the area mentioned. Questioning reveals absence of any other illnesses in the past history. She was married nineteen years and had nine children. She began to increase in weight steadily eleven years ago, following the birth of her first child. In functional enquiry, she admitted dyspnoea on exertion, one flight of stairs tiring her considerably. She also had slight swelling of the ankles at night. Other systems were apparently normal.

The patient was sixty-eight inches in height and weighed two hundred and forty-three pounds. General physical examination revealed the presence of dental caries, a heart slightly enlarged, and blood pressure was 153 | 105. The abdomen was protuberant, doughy, with absence of pain on palpation. A typical "catch" in the breath was elicited by deep pressure under the right ninth costal cartilage, the patient taking a deep inspiration. Repeated examinations of the urine gave negative results. The concentration of the haemoglobin was 85%, the erythrocytes numbered 4,500,000 and the leucocytes 8,100. Differential count was normal and the Wasserman reaction negative. Glucose tolerance tests were slightly above normal, and the blood urea and creatinine estimations were normal. Three basal metabolic rates gave an average of plus 4%. Phenosulphonethalein tests resulted in first specimen containing 44% of the dye and the second specimen in two hours, 35%. By means of X-ray and ingestion of iodeikon emulsion, the gall bladder showed no filling with the dye, no stones and absence of any gastric lesion. X-ray of the teeth revealed dental caries and alveolar absorption with the presence of several infected roots.

In such a patient as this one, the probable accepted factors, infection, stasis and hypercholesterolemia, are well exemplified. This patient, undoubtedly, has numerous foci of infec-

tion present, all productive of a low grade cholecystitis at any time, and thus predisposing of the formation of calculi. Mann has shown that the normal emptying time of the gall bladder does not occur in pregnancy, and that a condition of stasis exists which may play a part in the production of gall stones. This particular patient is fat, female and forty, has had nine pregnancies, and thus has undoubtedly had a high blood cholesterol on numerous occasions serving to initiate calculus formation.

The most striking feature on first observation of this patient is her obesity. In considering this aspect, we must remember obesity is of two types, endogenous and exogenous. The former may be divided into three classes (a) hypothyroid (obviously, this patient is not of this group, as shown by examination and basal metabolic readings); (b) pituitary class in adolescents which is an anterior lobe dyscrasia; (c) pituitary class in adults in which there is an increase in girdle fat and a disproportion between girth of abdomen and that of shoulders. This patient does not show this phenomenon, the glucose tolerance tests are high but not diabetic, and X-ray of the skull is as follows —"The sella turcica appeared normal in size and shape, with no evidence of irregularity in the pituitary mass." Thus, this was obesity which belonged to the exogenous type. To support this statement we find the patient was very fond of fats of various kinds, especially butter, and consumed large amounts of bread. Von Noorden has said that two hundred calories extra in a diet a day for one year would increase the weight of a person as much as twenty-four pounds. The ability to eat naturally depends on appetite, and associated with pregnancy one often finds an increased appetite (as she had) with resulting increase in consumption of calories.

The association of obesity, arteriosclerosis and gall stones one with another is common enough and so in this woman further investigation was carried out. In routine examination of radial and brachial vessels no palpable tortuosity or beading could be felt. However, by means of soft tissue technique, X-Ray showed the peripheral vessels to be thickened and tortuous with calcification in relation to the vessels of the calves of both legs, a degree of arteriosclerosis being present which is rather unusual in a patient of forty-two years. As mentioned before, the heart was slightly enlarged to percussion, the hypertrophy possibly being a response to the strain of an early consistent rise in diastolic pressure. The electrocardiographic tracing showed left axis deviation, negative waves in second and third leads, split Q.R.S. complex, indicating severe myocardial damage.

In considering the treatment to be given this patient, it was felt that the local condition of Chronic Gall Bladder disease was not urgent and general measures were instituted. She was allowed out of bed and urged to walk around the wards and exercise mildly. A suitable reducing diet was arranged, consisting of Carbohydrate 150 g., Protein 70 g., Fat 60 g., a total of 1,420 calories, the 70 g. protein adequately maintaining her nitrogen equilibrium. At this time, her weight was two hundred and forty-three pounds on November 16th, 1932. Three days later, a further reduction to C.120, P 70, F. 40 (1120 calories) was made and the patient continued along well satisfied with her diet. On November 25th, 1932, the diet was still further reduced to C. 110, P. 70, F. 40 (1080 calories) and her weight was now two hundred and thirty-eight pounds, a reduction of five pounds in nine days. Patient followed her diet carefully, satisfied her appretite and with gratifying results. She lost weight regularly at the rate of a half pound a day and improved with a general feeling of well being. In a patient so obese as this one, more rapid reduction in weight is undesirable

as appearance of facial wrinkles often occurs. On December 22nd, thirty-six days after the beginning of the diet, she weighed two hundred and twenty-three pounds, a reduction of twenty pounds from her initial weight. Thyroid extract Gr. 2 t.i.d. p.c. was given throughout this period with the idea of further speeding up her metabolism. As dental examination, together with X-ray, showed definite infection present, the teeth were extracted, 5-7 being removed each week under local anaesthesia.

In considering this case, the lesson to be derived is that the obvious pathological condition is not always that most requiring treatment. She was a fat woman admitted, following a gall bladder attack and our first reaction was to submit her to surgery and yet on further study she is found to have extensive arterial and cardiac damage and a lowered carbohydrate tolerance. She is obviously not a first class surgical risk. She has a pathological gall bladder, but her vascular disease is of much more importance. Towards the development of this and probably also to her gall bladder disease, her obesity has undoubtedly contributed much. It would appear reasonable, therefore, to first undertake weight reduction, the removal of focal infection, etc., and after an improvement in her general health has resulted, a cholecystectomy might then be considered.

THE RELATIONSHIP BETWEEN CANCER AND TUBERCULOSIS

By J. B. AIKEN, '33, AND A. A. ROGOW, '33.

The problem of cancer has been attacked from almost every conceivable angle. The relationships of cancer to other conditions have been extensively investigated. A few of these being, the relation of cancer to chronic irritation, use of chemicals, endocrine disturbance, pernicious anaemia and acute infections. An attempt has also been made to study cancer in its relation to tuberculosis. We shall attempt here a review of the literature and a discussion of this relationship.

Walshe, pathologist at University College Hospital ninety years ago, said that "tubercle and carcinoma possess a sort of repulsion in respect of each other," but attention was really attracted to the subject in 1855, when Rokitansky introduced the idea that cancer and tuberculosis were antagonistic diseases. He was later forced to admit that tuberculosis could be followed by cancer, but still maintained that cancer could not be followed by tuberculosis. He mentioned especially the fact that at the sites where tuberculosis frequently occurs, e.g., lung, cancer is only rarely found, and, conversely, the most favourite sites for cancer, e.g., esophagus, stomach, rectum and ovary, are only rarely the site of tuberculosis.

Since that time a great deal has been written on the subject, and more especially in recent years. The publications fall into three groups: (a) Case reports; (b) Experimental studies; and (c) Statistical studies.

(a) Case Reports.

Reports of cases have appeared of cancer and tuberculosis co-existing in the same body, and in the same parts of the body, such as lung, uterus, breast and larynx. A few cases of primary carcinoma in a tuberculous cavern of lung have also been reported. These cases show that the two diseases can

co-exist, but do not prove that there is no antagonism, because the cases are relatively few in number. Also, the affect of cachexia on the resistance of the body must be taken into account.

(b) Experimental Studies.

These fall into two groups: animal and human experimentation.

Centanni and Rezzesi experimented with mice which were 100% susceptible to a transplantable mouse adenocarcinoma. Mice with adenocarcinoma showed a somewhat greater resistance to bovine tubercle bacilli than did controls. No tumors could be produced by simultaneous injection of tubercle bacilli and cancer in the same place. Previous injection of tubercle bacilli delayed the development of the tumor. Injection of live tubercle bacilli into a tumor mass caused it to be partially destroyed. Dead bacilli had no effect on the tumor. Tuberculin injected along with the tumor emulsion retarded or inhibited its growth. The experiments they performed were too few in number from which to draw definite conclusions.

Tuetschlaender experimented with mice susceptible to Rous Sarcoma and tuberculosis. He found that the presence of tuberculosis in these animals interfered with the growth of the Rous Sarcoma. He believes that the antiblastic action of the tuberculosis is an indirect or systemic one, and not a direct bacteriotoxic action on the cancer cells. It has been shown that tubercle bacilli per se do not injure a culture of Rous Sarcoma. The bacilli were phagocyted by the Sarcoma cells, from which subcultures could be successfully made for more than a year.

Although cancer cells are destroyed in the presence of tuberculosis, this has little significance, because other toxic agents will do the same. These experiments tend to show that the growth of tumor is delayed by the presence of active tubercle bacilli, but not prevented.

An entirely different view has been taken by Cherry of Australia, who has done considerable experimental work with mice. He has shown that the injection of tubercle bacilli into mice will produce new growths in the pancreas. He states that cancer can develop at a tuberculous site, and attaches a great deal of importance to the presence of the lymphocytic reaction present about tuberculous foci, which, he says, predisposes to the development of malignancy.

Experiments on human patients dying from cancer have been few. Mc-

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Caskey suggested trying the injection of tuberculin into the tumor in inoperable cases. In 1916, Dabney treated seven such cases with tuberculin. Two of these showed a marked improvement in three months, but he was unable to follow the cases further. Sutton and Pearl, in 1928, found that tumors treated with tuberculin showed definite retrogression with improvement in general condition. Teutschlaender now proposes the use of tuberculin in treatment of cancer cases.

(c) Statistical Studies.

It is a well-known fact that tuberculosis is more prevalent in early life while cancer is essentially a disease of later life; also, that cancer deaths are increasing while deaths from tuberculosis are decreasing.

Lubarsch in 1888, in 6,536 post mortems, found that cancer was twice as common in non-tuberculous patients, as in those with active tuberculosis. He determined that tuberculosis was one-and-a-half times as frequent in non-cancerous as in cancerous patients. His figures, however, were not sufficiently controlled by age limits.

Pearl studied a similar series of cases but eliminated possible errors by rigid controls with respect to age, sex, color and time of death. Tuberculous lesions found in control cases were two-and-a-half times as frequent as in cancer cases. Cancer in non-tuberculous cases had an incidence eight times that of cancer in cases of florid tuberculosis. Healed tuberculosis was found to occur as frequently in cancer cases as in controls, but active tuberculosis was found in 16.3% of controls and in only 6.6% of the cancer series. He concludes: "Only rarely does an active and considerable tuberculosis exist with a malignant neoplasm in the same individual. There appears to be a sufficient antagonism between these two pathological phenomena, which disappears when and if the tuberculous process retrogresses or heals, particularly by the fibrotic route." In his article he mentions the work of Levin, who found very few cases in which tuberculosis or syphilis co-existed with cancer. Levin also stated that not a single case of cancer was found among the lepers "notwithstanding the special research instituted into the matter."

Discussion.

From our study of the literature, we are inclined to believe that there is a definite antagonism between cancer and tuberculosis, although the few case reports of their co-existence, and the work of Cherry, might lead one to believe otherwise. Teutschlaender says this antagonism is not a specific one, but a non-specific or systemic one. Meyer believes that cancer is a systemic disease. Such a condition would tend to facilitate a non-specific antagonism. There seems also to be an antagonism between cancer and the granulomata of syphilis and leprosy. This might indicate that the antagonism is not specific, but is due to something common to these granulomata. From pathological studies we know that the granulomata are all characterized by their proliferative reaction. Now, we may ask, why does such an antagonism appear?

From the above experimental studies it is noticed that viable tubercle bacilli had some effect on malignant neoplasms, but tuberculin had little, if any. Why should tubercle bacilli injected into the body give a different result than tuberculin? To answer these two questions, we must digress a little.

Epithelial layers lining, skin and mucous membranes, etc., are supported on a connective tissue basement membrane. Normally these epithelial elements do not break through the basement membrane, but in carcinoma they do. The general belief to-day is that the basement membrane is supporting in nature, but histological study of normal tissues and carcinoma has led some to believe that it also exerts an inhibiting influence on epithelial overgrowth. This may be due to an antiplastic substance present or liberated

by the basement membrane, which property is perhaps common to all connective tissue. The epithelium in opposition probably secretes a plastic substance tending to make its cells proliferate. Thus a balance between the action of the plastic and anti-plastic substances on the epithelial cells is normally present. With a disturbance of this balance due to a diminution of the anti-plastic substance epithelial overgrowth and invasion may occur.

In any inflammatory condition in which there is a connective tissue proliferation tending to localize the process, this tissue, together with the connective tissue about it, would tend to produce an increased amount of antiplastic substance. This type of reaction is seen in the granulomata, especially in the specific granulomata of tuberculosis, syphilis and leprosy. A similar connective tissue reaction is often seen about invading masses of cancer, but it is probably not sufficient to wall it off.

In the light of this theory, originated by B. Cohen of Toronto, the answers to the above questions are self-evident. Tubercle bacilli, when injected into a mouse, causes the formation of a tubercle, and perhaps produce this theoretical antiplastic substance. Tuberculin injected into a mouse free from tuberculosis occasions no such reaction, and therefore produces no antiplastic substance.

Cases have been reported where cancer developed secondary to tuberculosis. This could be perhaps explained by saying that there was such marked cacnexia of the body due to the cancer that the tissues would not react sufficiently. Similarly, one could explain the occasional development of tuberculosis secondary to the development to malignancy.

If such an antiplastic substance were produced in the body it might probably be found in exudates in tuberculous pleural of tuberculous joint effusions, or in any other proliferative type of inflammation, thus it might be made available for experimental purposes.

In conclusion, may we say that this view of plastic and antiplastic substances, etc., is purely theoretical, and, as far as we know, no experimental work has been done along such lines.

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THE DOCTOR'S PRACTICAL RELATION TO THE CANCER PROBLEM*

By W. C. MacCARTY, M.D.

The cancer problem has many phases, such as histogenesis, etiology, immunity, and heredity, which are being studied in institutions for pure research. But aside from these subjects, still open to investigation, there are three immediate and practical phases about which much is already known: the frequency of the disease, the necessity of and means of early diagnosis, and the good results of present methods of treatment. With the general acceptance of this knowledge cancer can easily be materially reduced in seriousness. In so far as medical students and practitioners are concerned, the immediate and tangible problem rests in effectual utilization of this knowledge for practical purposes.

Statistics reveal that there are approximately 150,000 deaths from cancer yearly in the United States. The more important problem is to reduce this number and to care for those victims who are still alive. By calculation I have decided that there are at least 2,000,000, and possibly more, cancer patients in our midst who are waiting to be recognized. Statistics reveal that 75 per cent. of the cancers of the stomach are inoperable when the patients are first seen in consultation by the surgeon (Balfour). This leaves only 25 per cent. to whom some possibility of help can be offered. Even this 25 per cent. does not represent the early stages of cancer; by actual measurement it is found that the resected gastric cancers average 6 cm. in diameter, 50 per cent. of these being palpable through the abdominal wall (MacCarty). With increasing knowledge, and more general use of the roentgen rays, we are, however, seeing an increasing number of smaller lesions but no more than are required to show that there is much room for improvement. What has been said of gastric cancer is also true of cancers in other regions. Thus, 30 to 50 per cent. of the cancerous breasts and 25 per cent. of the large intestinal cancers are inoperable, according to Harrington and Rankin. The average size of the operable lesions is 3 cm. for the breast and 6.5 cm. for the large intestine (MacCarty). There must be reasons why these cancers are so large. Certainly all of them have not been symptomless and many of the patients have been seen by physicians, or by venders of various medicines for temporary relief of symptoms. Possibly there are six reasons:

1. The patient with cancer does not always know that he or she is even sick. This certainly happens, but rarely.

2. The patient suspecting cancer fears an examination. This happens, but probably less frequently than ten years ago.

3. The patient does not submit to complete examination. This happens frequently because not 25 per cent. of the patients with cancer of the stomach, encountered in Kirklin's experience, have been previously subjected to roentgenologic examination.

4 The patient goes to a physician and it is actually impossible for him to recognize the condition. This occurs.

5. The patient refuses to take the physician's advice. This occurs, but not as frequently as in past years.

6. Early cancer does not give the text-book signs and symptoms of cancer, but rather those of chronic inflammation, obstruction of some kind, anemia, hemorrhage, or weakness.

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In my opinion the medical profession is suffering from a confusion of knowledge largely the result of a confusion of nomenclature, premature theoretical explanations, some stubbornness, and impractical conservatism. There are more than 950 terms used to name neoplastic conditions. As a matter of fact there are only three great groups of neoplasms in so far as their cytology and clinical behavior are concerned (MacCarty):

1. Those composed of adult cells with normal tissue arrangement: the *cytomas.*

2. Those compased of cells normally or nearly normally arranged but having the morphology of malignant regenerative cells: the *blastomas*

3. Those composed of cells of the malignant regenerative type, not arranged in any fashion approaching that of any normal tissue: the *problastomas.*

It may be said that the first two groups have their subdivisions, but these are only of academic interest and have the same diagnostic and prognostic significance as their respective main groups.

Clinical experience has taught us that the neoplasms of the first group are relatively benign, in that they are not invasive, grow by expansion, and do not metastasize. They sometimes kill by impinging on or interfering with vital structures. The second and third groups are clinically malignant, in that they invade surrounding tissues and form regional and distant metastatic growths. The general popular term "cancer" embraces the second and third groups, but not the first.

For each group there are many synonyms. Such a superfluity of names is naturally the result of that great period of observation and collection of material which has always necessarily been the forerunner of scientific generalizations.

Although each of the three main groups (the cytomas, blastomas, and probdastolas) has its own general and variable prognosis, there are still other factors which alter or control the prognosis in individual cases. Each of these, and there may be more, has been studied, and there are enough facts to aid us materially in handling our problem.

Factors Governing Prognosis.

Judging from my own clinical and pathological experience there are at least fifteen factors governing prognosis in cancer. I shall describe them briefly in the approximate order of their clinical importance.

1. *The presence or absence of nodal involvement and distant metastasis.* It may be stated that length of life is inversely proportional to the amount of nodal involvement and distant metastasis. To this principle there is the corollary that the proximity of death depends also on the vital anatomic situation of both primary growth and metastasis. In support of this first principle many figures might be given. I shall, however, confine myself to a few of the statistics from The Mayo Clinic.

Table 1.

NODAL INVOLVEMENT.

Organ.	Cases studies.	Length of post-operative life, years.	With nodal involvement, per cent.	Without nodal involvement, per cent.
Breast .	962	3	39.25	74.6
Stomach.	1000	3	19.00	52.0
Breast .	962	5	24.2	63.5
Lip	136	5	18.1	90.3
Breast .	218	5 to 8	18.9	63.9
Breast .	962	10	13.3	44.0

2. *Fixation of growth.* The greater the fixation of a cancer to surrounding structures, the greater the difficulty of surgical removal, the greater the immediate operative risk, the greater the chance of local recurrence, and the less the chance of complete recovery. I have no figures to substantiate this principle, but practical experience shows that surgeons will not attempt removal of a fixed growth. Such patients are referred to radiologists.

3. *Situation.* Cancers situated in organs that are easily accessible at physical examination, especially when the patient is forced to an examination by the presence of a tumor hemorrhage, pain, or obstruction, usually receive early

treatment and this is conceded universally by all to give the best prognosis. It may be stated, therefore, that malignant or benign tumors so situated as to produce early pain, hemorrhage, mechanical obstruction, or an easily recognizable mass, are more favorable. The relation of organic situation to size and favorability of early recognition may be seen in Table 2 which represents a study of 3,778 cancers of the large bowel, breast and stomach (MacCarty).

Table 2.

RELATION OF SITUATION TO SIZE.

Situation.	Average size, cm.	Largest, cm.	Smallest, cm.
Hepatic flexure . .	8.94	14	4.0
Cecum	7.8	15	3.0
Ascending colon . .	7.26	14	4.0
Transverse colon .	7.22	14	2.0
Stomach	6.16	19	0.5
Descending colon .	6.07	13	2.0
Rectosigmoid and sigmoid	5.94	15	1.0
Splenic flexure . . .	5.9	8	2.0
Rectum	5.8	18	1.5
Breast	3.2	13	0.2

In general it may be stated that the greater the diagnostic and therapeutic accessibility of a growth and the earlier it produces incapacitating signs and symptoms, the better the prognosis.

4 and 5. *Renal and cardiac efficiency.* The part which the heart and kidneys play in cancer is similar to that which they play in general health. The lower the cardiac and renal efficiency the poorer the prognosis, and especially the greater the immediate therapeutic risk.

6. *Anemia.* This condition is associated apparently with two different conditions: reduction of diet and single hemorrhage or constant or repeated oozing from the growth. Perhaps a third condition exists, although it is difficult to prove that it is not one of the two. By this I mean anemia due to a theoretically existent toxic condition arising from the cancer itself, or associated with its disintegration. In general, it may be said that, the greater the anemia the greater the immediate therapeutic risk and the shorter the life. If, however, the anemia is the result of a single or of recent repeated hemorrhages from the growth, this may not necessarily alter the ultimate prognosis after the growth is removed.

7. *Size of growth.* In my experience, a long enough period has not elapsed since accurate measurements have been made to allow definite conclusions. Information, therefore, must be indirect. It has been established that there is a definite relationship between the size of growth and the presence of nodal involvement which in turn has prognostic value. In table 3 the relationship of size of growth to the presence of nodal involvement may be seen.

Table 3.

RELATIONSHIP OF SIZE OF GROWTH TO NODAL INVOLVEMENT.

Organ.	Cases	With nodal involvement, cm.	Without nodal involvement, cm.
Hepatic flexure.	16	8.55	9.34
Cecum	118	7.8	7.8
Transverse colon	61	6.85	7.6
Stomach	1002	6.74	5.58
Splenic flexure .	10	6.4	5.4
Rectosigmoid and sigmoid.	469	6.04	5.84
Rectum	601	5.98	5.63
Descending colon	30	5.88	6.27
Ascending colon	28	5.6	8.92
Breast	1443	3.92	2.53
Total	3778		

In the first five organs or portions of organs, cancers are usually very large. There is no apparent relationship between size of growth and lymph nodal involvement in these, but in such organs as the rectosigmoid, splenic flexure, rectum, stomach and breast, where symptoms and signs appear early and are more easily recognized, there is a definite relationship. It is fair to state that the larger the primary growth the greater the possibility of nodal involvement, and hence the worse the prognosis.

8. *Age.* It is the general clinical impression that age has some bearing on the prognosis. Thus, clinical experience reveals that cancer is usually more rapidly fatal to a young person than to an older person. It is very difficult, how-

ever, to study this problem statistically because many other factors are involved. If age alone is taken into consideration there may be still a difference of size, situation, fixation, duration, character of growth and nodal involvement, to say nothing of general factors such as pulmonary, cardiac and renal efficiency. In a series of 218 patients with cancer of the breast who died of recurrence, Sistrunk and I reported that 41.7 per cent. of those who were more than fifty years of age were alive from five to eight years after operation and that 31.8 per cent. of those who were less than fifty were alive for the same period. These figures confirm the general opinion. On the other hand, in studying the same series in decades we found many variations.

Table 4.

AGE.

Decade of life, years.	Units.	Post-operative length of life. Patients without nodal involvement. Average.	Longest.	Shortest.	Patients with nodal involvement. Average.	Longest.	Shortest.
	Years	3	4	3	2	4	0
30 to 40	Months	5	5	0	3	9	5
	Days	19	2	22	16	3	18
	Years	2	3	1	2	7	0
60 to 70	Months	7	9	8	3	1	8
	Days	23	20	22	10	0	5

It appears that no great generalization should be drawn as to any constant differences in the different decades in this series. I believe that generalizations regarding age alone, when applied to clinical practice, might sometimes be very misleading. I have seen patients less than thirty years of age with cancer of the breast, rectum and ovary, all live more than twenty years after radical treatment. Despite the fairly common exceptions, it is perhaps correct to say that the younger the patient the worse the prognosis, keeping always in mind that all other factors have an influence regardless of age.

9. *Direction of growth.* By this expression it is meant to denote whether the bulk of the cancerous mass is toward the lumen or surface of the organ or whether it is infiltrating the wall and growing toward adjacent organs or cavities, such as the peritoneal cavity in the case of intestinal cancers or the thoracic cavity in the case of cancer of the breast. Some cancers, especially of the colon and stomach, grow massively toward the lumen, with little or no invasion of the wall. Others do not grow toward the lumen but invade the wall, the serosa, and the neighboring structures. Of the two types, the latter has the worst prognosis. It is more likely to be accompanied by nodal involvement, and may be much smaller than those which grow toward the lumen.

10. *Loss of weight.* There are probably several reasons for loss of weight in association with cancer: quality and quantity of food, mechanical obstruction, pain, worry, and possibly infection and absorption of disintegrating tissues. As a single prognostic factor it is probably of little significance, but taken in association with other factors it adds gravity to any prognosis. It must be kept in mind always that persons who are underweight are usually better surgical risks than those who are overweight.

11, 12, 13, and 14. *Cellular differentiation, lymphocytic infiltration, fibrosis and hyalinization.* Differentiation is undoubtedly important, but not as important as some clinicians have thought. It is of great scientific interest, but in considering its immediate clinical value, one must not forget that there are some exceptions to the general rule that favorability of prognosis is proportional to the degree of differentiation. There can be no doubt that there is some relation between the degree of differentia-

tion of tumor cells and their rate of growth, but rate of growth is variable even in the same tumor. Size situation, infiltration, nodal involvement, fixation, lymphocytic infiltration, fibrosis and hyalinization must all be taken into consideration.

of value taken in conjunction with other factors.

Now, before concluding, something practical relative to the frequently used term "biopsy" should be stated:

The term is used ordinarily to mean microscopic visualization of tissue re-

Table 5.

RELATIONSHIP OF PRESENCE OF NODAL INVOLVEMENT AND SIZE.

Organ.	Cases.	Size, cm. Largest.	Smallest.	Average.	Percentage with nodal involvement.
Grade 4—					
Stomach	55	15	3.0	7.8	85.0
Breast	72	13	1.0	5.4	75.0
Colon and rectum	10	9	5.0	4.4	80.0
Grade 3—					
Stomach	67	15	2.5	5.8	62.0
Breast	53	7	1.0	3.25	58.0
Colon and rectum	58	15	3.0	6.1	77.0
Grade 2—					
Stomach	25	16	1.8	6.7	12.0
Breast	32	12	0.8	3.4	18.7
Colon and rectum	138	13	1.0	5.6	35.0
Grade 1—					
Stomach	1	7	7.0	7.0	0.0
Breast	0	0	0.0	0.0	0.0
Colon and rectum	21	11	1.5	4.9	9.5

15. *Duration of disease.* Nothing is more inaccurate and unreliable than the recorded duration of disease in most written histories of cancer. Duration is more important when applied to individual signs and symptoms, which unfortunately have nothing to do with the type or grade of cancer itself. Signs and symptoms in cancer have to do with size, anatomic situation, mechanical obstruction and hemorrhage. Even pain is usually insignificant unless associated with mechanical obstruction None of these is diagnostic of cancer, or even prognostic if treatment can be instituted. Many benign conditions present such signs and symptoms, and may have been present long before cancer has arisen. In other words, it is often impossible to decide or determine the duration of the actual malignant growth in the great majority of instances. As a single prognostic sign it has little value. Inoperable cancers, especially of the stomach and colon, frequently have very short recognizable histories. In general, the duration of the disease is mainly moved during life. Four functions are served by the procedure: differential clinical diagnosis, research, prognosis and the direction of treatment. Of these the first and last are at present of greatest practical importance. Since there are no reliable clinical or serologic tests for the recognition of cancer in its early stages and since cancer is frequently associated with chronic inflammatory conditions which give signs and symptoms, experience has taught that biopsy is the only means of making a differential diagnosis in many instances. The situation has been made simpler by perfection of surgical technic and by the utilization of pathologists as necessary clinical adjuncts to the practice of medicine and surgery. The risk of removing tissues is almost nothing when it is done by well trained and experienced surgeons. In clinical practice, dealing with attempts to treat cancer in its early stages, the following rules have been of value:

1. Every chronic sore or lump, especially if recently acquired, which does

not disappear or become smaller, or show signs of disappearance after two or three weeks of local treatment (rest, local antiseptic care and general hygenic care) should be subject to biopsy. It should be excised if possible rather than incised.

2. Tissue for biopsy should not be removed unless the one who removes it is capable of performing the radical operation in case a malignant condition is found, or unless he is in close proximity to some one capable of completing the operation.

3. The biopsy should not be performed, as a rule, on small, doubtful lesions situated near epiphyseal lines in children. There are, perhaps, rare exceptions to this rule.

4. Biopsy should not be undertaken if the immediate and ultimate operative risks are greater than the possibility of cancer.

5. Tissue may be removed by incision of the sore or lump, if it is large, and if it is thought to constitute a hopeless condition in which there is only a small chance that the lesion is not malignant. Immediate radical operation should follow the diagnosis if experience shows that radical operation will prolong useful life or that it will make even a short life free from lingering suffering; otherwise it is unnecessary.

6. Biopsy may be done by means of surgical exploration of body cavities in which some unrecognizable but incapacitating pathologic condition is known to exist. Differential clinical diagnosis of conditions of the abdomen, bones and central nervous system is becoming more difficult, and experience with surgical exploration shows that many small cancers are being found. In the hands of well-trained surgeons risks of exploration are relatively small. The conservative surgeon is likely to refrain from exploration unless the patient is at least partially incapacitated, unless roentgenologic studies reveal a definite lesion in one of the systems, or unless, even though roentgenologic signs are absent, the patient's incapacity is increasing despite ordinary nonsurgical treatment.

Material removal for biopsy is studied best at the time of operation, and in a fresh, unfixed condition. It may be fixed, cut by the frozen tissue method, and stained, or it may be embedded in paraffin or cellodin, cut and stained in the usual manner. The first of these (fresh and unfixed) is the best in the hands of those especially trained in living cytology; fine details of cellular morphology are lost after fixation and embedding, leaving only histologic criteria by which the nature of the specimen can be judged. I feel, after long experience with all methods, that the fresh tissue method gives about 10 per cent. greater chance of recognition of early cancer.

In conclusion, may it be said that progress in handling the cancer problem rests, for the present at least, on more complete examinations (especially with roentgen rays and biopsy), the recognition of the fact that early cancers do not give symptoms of cancer as described in text books, the general acceptance of the relationship of chronic inflammation to cancer, and the elimination of much if not all of our confused and not universally accepted terminology. If these simple and established facts form an intimate part of the practitioner's system of dealing with all patients, then he will surely discover many early cancers and properly care for the 2,000,000 or 3,000,000 which are now waiting to be recognized. There is no use talking about "early diagnosis" and then expecting to make diagnosis in this stage by signs and symptoms of cancer. The various organizations for the dissemination of knowledge to laymen have done their work well.

CANCER OF THE STOMACH*

By J. SHELTON HORSLEY, M.D.

Deaths from cancer are increasing. There are now in the United States about 120,000 deaths from cancer each year, one-fourth to one-third of them being from cancer of the stomach.

In the fight against cancer, the most powerful of the captains of the men of death is cancer of the stomach.

Gastric cancer occurs more frequently in men than in women. Clinically it may be divided into two classes: (1) the kind of cancer that gives a history of indigestion, frequently resembling the history of peptic ulcer, for several years before the cancer becomes obvious; (2) the cancer of the stomach in which gastric symptoms appear only a few months before the disease is detected. The first type represents about 25 to 30 per cent. of all gastric cancers. The second type comprises about 70 to 75 per cent. of the gastric cancers.

Elsewhere in the body it seems to be true that cancer does not originate directly from normal healthy tissue. In regions that we can inspect, as the mouth, tongue, skin, rectum and lower sigmoid, cancer arises on a pre-existing benign lesion such as a patch of leukoplakia, a wart, a mole, an ulcer or a polyp-like growth. It is probable that cancer in the stomach follows this same general law. In the interior of the stomach, which cannot be satisfactorily inspected, benign growths or even ulcers may exist for years, especially if in the "silent areas" of the stomach, without creating symptoms until cancerous change and rapid growth have set in. The lesser curvature of the stomach, where gastric peristalsis begins, is the important motor region and about 80 per cent. of all stomach complaints are due to interference with its peristalsis. A growth or lesion of any kind in the narrow pyloric end of the stomach may also cause symptoms because of partial obstruction. Roentgenologists say that any ulcer along the greater curvature of the stomach capable of demonstration by X-ray is practically always malignant, while many of the ulcers on the lesser curvature are benign.

It is generally recognized that some gastric cancers have their origin in benign peptic ulcers The ratio of this incidence, however, is a subject of much dispute. It is true, too, that there is a low-grade cancer of the stomach which ulcerates early and cannot be distinguished grossly even at operation from a benign ulcer, microscopic examination being necessary to make a diagnosis. In the opinion of Holmes and Hampton, roentgenologists of the Massachusetts General Hospital, and of many gastro-enterologists, the difficulty in differentiating between early cancer and peptic ulcer is so great as to call for surgical excision, the only known means of curing gastric cancer, unless the suspected lesion responds to medical treatment within a few weeks.

Because of the proximity of the liver and pancreas to the stomach and because, also, gastric cancers are usually not very radio-sensitive, efficient radiation treatment cannot be given gastric cancer, so the only means of cure is excision by partial gastrectomy. In some rare instances a total gastrectomy is justifiable.

If a patient reaches the "tropic of cancer," say 35 years of age, and begins to complain of vague symptoms of indigestion, such as belching, nausea, water-brash, heart-burn, sometimes vomiting, pain and discomfort in the upper abdomen, whether coming on at a regular time after meals or not, he should receive a careful examination

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by a competent general practitioner. In the majority of cases this stomach trouble will be found to be due to something other than a gastric lesion, and can be cured by appropriate medical measures. If, however, the patient is not relieved of his complaints after faithfully following the advised treatment for two or three weeks, his stomach and intestines should be examined with X-rays by someone fully competent to do this.

If cancer is found, an operation should be done as soon as possible by a surgeon of experience in gastric surgery. If the lesion appears to be a peptic ulcer, medical treatment may be instituted for a few weeks; then, if improvement as noted by X-rays and clinically is not marked, the lesion should be removed by a partial gastrectomy.

If the patient has been having stomach symptoms for many years, and reaches the age of 35 years, the same routine should be enforced.

In the early stages of disease the diagnosis is difficult, but it is in the early stages that the diagnosis is important so that proper treatment can be given. It has been shown by Dr. Margaret Warwick that in about 23 per cent of cancers of the stomach coming to necropsy the cancer is still confined to the stomach, and that many of these deaths result from perforation of the cancer and peritonitis, and not from the constitutional effects of cancer. It seems probable that, if at necropsy 23 per cent. of gastric cancers are still limited to the stomach, an earlier diagnosis and a proper operation would uncover a larger percentage of cases in which the cancer was confined to the stomach and could be cured by partial gastrectomy.

It is only by adopting some plan to follow through to a definite diagnosis and treatment the earliest signs of stomach trouble that the enormous mortality from gastric cancer can be reduced.

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